Statement of the Infectious Diseases Society of America (IDSA) Concerning Project Bioshield Reauthorization Issues
Presented by Martin J. Blaser, MD
Before the U.S. House Energy and Commerce Committee's
Subcommittee on Health
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Chairman Deal, Ranking Member Brown and Members of the Subcommittee, thank you for inviting the Infectious Diseases Society of America (IDSA) to present our views on how best to strengthen Project Bioshield as the Subcommittee considers its reauthorization. I am Dr. Martin J. Blaser, President of IDSA and a Frederick H. King Professor and Chair of the Department of Medicine, and Professor of Microbiology at NYU School of Medicine.

IDSA represents 8,000 physicians and scientists devoted to patient care, education, research, prevention, and community health planning in infectious diseases. Our members care for patients of all ages with serious infections, including antibiotic-resistant bacterial infections, meningitis, pneumonia, tuberculosis, food poisoning, HIV/AIDS, and those with cancer or transplants who have life-threatening infections caused by unusual microorganisms, as well as emerging infections like severe acute respiratory syndrome (SARS). Housed within IDSA is the HIV Medicine Association (HIVMA), which represents more than 3,200 physicians working on the frontline of the HIV/AIDS pandemic. HIVMA members conduct research, implement prevention programs, and provide clinical services to individuals that are infected with HIV/AIDS. Together, IDSA and HIVMA are the principal organizations representing infectious diseases and HIV physicians in the United States.

I am testifying today on behalf of IDSA to highlight the critical need for new drugs, vaccines and diagnostics to treat, prevent and detect infectious diseases agents. As Members of the Subcommittee move forward to consider the reauthorization of the Project Bioshield Act, IDSA urges you to extend the statutes' scope beyond products intended to address bioterrorism-related pathogens and apply current incentives to products to be used against naturally occurring infectious diseases, including antimicrobial resistant infections. We also ask that you add several new provisions to Bioshield that will help to eliminate disincentives and to spur infectious diseases product development both related to naturally occurring infections and biodefense.

Members of the Energy and Commerce Committee have shown that they understand the connection between naturally occurring infections and bioterrorism and understand our nation's vulnerability. In its 2003 Committee report on the Project Bioshield Act, the Committee linked *natural conditions*, including antimicrobial resistance and dangerous viruses, to national security concerns. The Report stated "advancing the discovery of new antimicrobial drugs to treat resistant organisms … may well pay dividends for both national security and public health."

IDSA believes that there is an inextricably linked, synergistic relationship between the research and development (R&D) needed to protect against both natural occurring infections and bioterrorism agents. Research in both areas seeks to understand how these organisms cause disease, the immune system response to these pathogens, the development of drug resistance, and how antibiodies and medicines protect against them. Moreover, antibiotic resistant organisms that currently threaten Americans in hospitals

and communities can have future national and global security implications. Virtually all of the antibiotic-resistant pathogens that exist naturally today can be bio-engineered through forced mutation or cloning. Expanding the government's product development priorities to include naturally occurring infections will enhance the research needed to develop bioterrorism countermeasures and vice versa.

Background

On July 21, 2004, the same day that President Bush signed "The Project Bioshield Act", IDSA issued its landmark report entitled, *Bad Bugs, No Drugs, As Antibiotic Discovery Stagnates, A Public Health Crisis Brews.* Copies of that report are available here today. Our report calls attention to a serious public health problem—at the same time that emerging infections and antibiotic resistance are increasing, drug companies are withdrawing from antiinfective R&D. IDSA is particularly concerned about antibiotic R&D, an area in which many pharmaceutical and biotechnology companies have shown the least commitment in recent years, either withdrawing totally or seriously downsizing their dedicated resources and staff.

Let me be very clear from the start: IDSA is here today on behalf of patients. We are not here at the request of the pharmaceutical or biotechnology industries nor is our *Bad Bugs, No Drugs* advocacy campaign financed in any way by industry. Infectious diseases (ID) and HIV physicians on the frontline of patient care see patients every day who face lengthy and expensive hospitalizations, painful courses of treatment and even death because of drug-resistant and other infections. We are here because our patients desperately need new weapons to protect them against these diseases.

Why Policymakers Should be Concerned

Policymakers have recognized the urgent need to spur biodefense R&D, which led to the establishment of Project Bioshield. While concern about bioterrorism is appropriate, it is important to keep things in perspective. Not one American has died from bioterrorism since President Bush first announced Project Bioshield in February of 2003, but drug-resistant bacterial and other infections have killed hundreds of thousands of Americans in hospitals and communities across the United States and millions of people across the world during that same short period of time.

Here are some surprising facts about the impact of drug-resistant bacterial infections in the United States:

- Antimicrobial resistant infections have created a "silent epidemic" in communities and hospitals across the country—methicillin-resistant staphylococcus aureus (MRSA), for example, is crippling and killing a growing number of athletes, children, military recruits, and prisoners.
- Infections caused by resistant bacteria can strike anyone—the young and the old, the healthy and the chronically ill. Theresa Drew recently shared the story of her son, Ricky Lannetti, with congressional staff. Ricky, a healthy and strong 21-year old college football player from Philadelphia, Pennsylvania succumbed to an MRSA infection in December 2003. Ricky's story is just the tip of the iceberg.
- About 2 million people acquire bacterial infections in U.S. hospitals each year, and 90,000 die as a result. About 70 percent of those infections are resistant to at least one drug. Community-acquired resistant infections also are on the rise. The

trends toward increasing drug resistance in both hospitals and communities show no sign of abating.

- Resistant pathogens lead to higher health care costs because they often require more expensive drugs and extended hospital stays. The hospital care for Bryce Smith, a 14-month old toddler from San Diego, cost more than $800,000 in the beginning months of 2006. The total cost of antimicrobial resistance to the U.S. health care system was nearly $5 billion in 1998, according to the Institute of Medicine (IOM). It is believed true costs far exceed that amount today.

What policymakers should know about pandemic influenza:

- The impact of an influenza pandemic cannot be overstated. The Centers for Disease Control and Prevention (CDC) estimates that between 100,000-250,000 U.S. deaths would result from a "mild" pandemic and 900,000–2 million Americans will die from a virus as deadly as the 1918 virus.
- The Congressional Budget Office estimated that a pandemic could cost $675 billion and decrease the real gross domestic product (GDP) by five percent.
- H5N1 avian influenza has spread rapidly in the past few months to more than 40 countries in Asia, Africa, the Middle East and Europe. Experts agree that it is only a matter of time before it appears among birds in North America.
- H5N1 virus is showing continued evolution, and has infected an increasing variety of mammals. A moderate number of human cases continue with a high death rate. Fortunately, the virus is not yet capable of easily spreading from person to person; should this happen, a dramatic pandemic will occur.

- Despite the increased attention and progress that has been made in preparing for an influenza pandemic, the Institute of Medicine and virtually all experts conclude that the United States is woefully unprepared to sufficiently respond to pandemic flu and many gaps and challenges remain.
- Moreover, seasonal influenza accounts for 36,000 deaths and more than 200,000 hospitalizations in the United States and 250,000 to 500,000 deaths globally each year.

Here are some important facts about other infectious diseases:

- Three of the biggest killers—HIV, tuberculosis (TB) and malaria—account for nearly 40 percent of deaths caused by infectious diseases (5.6 million deaths in 2002).
- Diarrheal diseases and respiratory infections are equally as deadly, accounting for 5.7 million deaths in 2002.
- More than three-dozen new infectious diseases have been identified since the 1970s that have impacted the United States and more vulnerable countries, including HIV/AIDS, SARS, West Nile virus, Lyme disease, hepatitis C, a new form of cholera, waterborne disease due to *Cryptosporidium*, foodborne disease caused by *E. coli* 0157:H7, and a plethora of neglected diseases that primarily affect patients in the developing world.

The Product Pipeline is Drying Up

Infectious diseases are the second leading cause of death in the world and, by far, the leading cause of premature death and disability. Unfortunately, many of these diseases have no treatment except for supportive care. New medicines and diagnostics are desperately needed across all areas of infectious diseases medicine.

Of particular concern, the pipeline of new antibiotics is drying up. Major pharmaceutical companies are losing interest in the antibiotics market because these drugs simply are not as profitable as drugs that treat chronic, life-long conditions and lifestyle issues. The pharmaceutical pipeline is not keeping pace with drug-resistant bacterial infections, so-called "superbugs." Antibiotics, like other antimicrobial drugs, have saved millions of lives and eased patients' suffering. The withdrawal of companies from antibiotic R&D is a frightening twist to the antibiotic resistance problem and, we believe, one that has not received adequate attention from federal policymakers.

A recent analysis published in the journal *Clinical Infectious Diseases* found only five new antibiotics in the R&D pipeline out of more than 506 drugs in development. The authors evaluated the websites or 2002 annual reports of 15 major pharmaceutical companies with a track record in antibiotic development and seven major biotechnology companies. Their analysis revealed four new antibiotics being developed by pharmaceutical companies, and only one antibiotic being developed by a biotech company. By comparison, the analysis found that the pharmaceutical companies were developing 67 new drugs for cancer, 33 for inflammation/pain, 34 for metabolic/endocrine disorders, and 32 for pulmonary disease. The biotech companies

were developing 24 drugs for inflammation/immunomodulators, 14 drugs for metabolic/endocrine disorders, and 13 for cancer.

The end result of the decline in antibiotic discovery research is that the Food and Drug Administration (FDA) is approving few new antibiotics. Since 1998, only 13 new antibiotics have been approved, two of which are truly novel—i.e., defined as having a new target of action, with no cross-resistance with other antibiotics. In 2002, among 89 new medicines emerging on the market, none was an antibiotic.

The Institute of Medicine's (IOM) 2003 report on microbial threats reinforces the point, noting that although at first glance the situation with respect to antibiotics currently in clinical development looks encouraging, not one *new class* of antibiotics is in late-stage development. "Rather these 'new' antibiotics belong to existing classes, including macrolides and quinolones, that have been used to treat humans for years," IOM said.

Unfortunately, both the public and private sectors appear to have been lulled into a false sense of security based on past successes. The potential crisis at hand is the result of a marked decrease in industry R&D, government inaction, and the increasing prevalence of resistant bacteria.

IDSA has investigated the decline in new antibiotic R&D for more than three years, interviewing stakeholders from all sectors. We have met with officials from FDA, the National Institute of Allergy and Infectious Diseases (NIAID), CDC, congressional members and staff, executives from leading pharmaceutical and biotechnology

companies, representatives from public-private partnerships that are focused on infectious diseases-related product development, patients, and other stakeholders.

Based on our investigation, IDSA is convinced that the pharmaceutical and biotechnology industries are clearly best situated to take the lead in developing new antibiotics needed to treat bacterial diseases. They are the only player with a track record of success. Consequently, industry action must become the central focus of an innovative federal public health effort designed to stimulate antibiotic R&D.

Some people have placed the blame for the decline in R&D on the pharmaceutical industry, saying that companies should act responsibly and ensure that new drugs and vaccines are available as needed. The pharmaceutical industry supports many good works *pro bono*. Some examples include Merck & Co.'s efforts related to River Blindness; efforts by Bristol-Myers Squibb, Pfizer, and other drug companies related to global AIDS; and GlaxoSmithKline's malaria and AstraZeneca's TB drug discovery initiatives. Nevertheless, companies are responsible to their shareholders and cannot alter their fundamental business strategies in ways that would place their bottom lines at risk.

Drug and vaccine R&D is expensive, risky, and time-consuming. As such, companies are most likely to invest in products for which a strong return on investment is likely, such as drugs that treat long-term, chronic illnesses, lifestyle issues, and products that benefit people in developed countries who can afford to pay for them. Most antiinfectives, particularly antibiotics, which are used for short durations (7-14 days), face restricted use to avoid the development of resistance, resistance limits effectiveness

and profitability, etc.; vaccines; and medicines desperately needed in the developing world are being left out.

Spurring Infectious Diseases Product Research and Development

Policymakers and the public should have no illusions that future pharmaceutical charity will be sufficient to address the existing and emerging infectious pathogens that threaten U.S. and global health. Instead, IDSA believes the burden is on the federal government to entice industry to antiinfective R&D as a means to protect U.S. public health and strengthen national security.

Robust R&D programs are needed to respond successfully to existing infectious diseases as well as new threats on the horizon. Market forces alone will not solve the current crisis in infectious diseases drug, vaccine and diagnostic R&D—that's why we need innovative public policy changes such as those that have been contemplated in the "Infectious Diseases Research and Development Act", a bipartisan bill introduced by Rep. Barbara Cubin last year. IDSA has strongly endorsed this bill and is particularly grateful to Rep. Cubin's commitment in this area. We encourage the Subcommittee to consider the bill as it moves forward to reauthorize Project Bioshield.

The "Infectious Diseases Research and Development Act" will provide incentives for pharmaceutical companies and biotechnology companies to invest in research and development with respect to antibiotic drugs, antivirals, diagnostic tests, and vaccines that may be used to identify, treat, or prevent *a "qualified infectious disease product."*

The bill defines a "*qualified infectious disease product*" as "any antibiotic drug, antiviral, diagnostic test, or vaccine that is developed for the purpose of treating, detecting, preventing, or identifying…an infectious pathogen identified by the [new] Commission [on Infectious Diseases Product Development, discussed below.]"

Prior to the establishment of the Commission and its initial report of infectious pathogens, the incentives outlined in the bill will be available in the interim to infectious diseases products addressing the following issues:

- methicillin-resistant staphylococcus areus—can infect the heart, bones, lungs, and bloodstream.
- life-threatening gram negative bacteria including, among others:
    - *Acinetobacter*, a type of bacteria that has caused stubborn wound infections in at 100 U.S. solders and civilians stationed in Iraq, and is an increasing cause of pneumonia in U.S. hospitals.
    - *Escherichia coli* and *Klebsiella* species, which are major causes of urinary tract, gastrointestinal tract, and wound infections.
- influenza–of particular note, the bill would entice the manufacture of products to treat influenza within the United States borders—an urgent need.
- Additional infectious pathogens as may be identified by the Secretary of Health and Human Services (HHS), in concurrence with infectious diseases clinicians.

As noted above, the bill establishes the Commission on Infectious Diseases Product Development. The Commission is required to identify the most dangerous infectious

disease pathogens and their associated diseases that are or are likely to become a danger to public health. The Commission would provide an annual report to Congress, the President, and the Secretary of Health and Human Services (HHS) on its findings, conclusions, and recommendations, including an updated list of emerging infectious pathogens.

Not later than 90 days after the date of enactment of the bill, the Commission also would be required to report recommendations on the actions the Secretary of HHS should take to ensure that a sufficient quantity of vaccines and anti-virals are available to treat the American population in the event of a pandemic influenza outbreak.

The Commission would be comprised of 19 voting members appointed by the President; 12 members to be appointed from among the leading representatives of the infectious disease medical, research, pharmaceutical, and biological communities, 7 members from the general public; additional nonvoting members would be appointed from the leading federal health agencies.

The Cubin bill also includes several incentives to spur R&D for qualified infectious diseases products that IDSA supports. Pathogens/diseases identified by the Commission as priorities for action would be eligible for these incentives. IDSA supports that following incentives:

- Full restoration of patent terms to account for the time lost during FDA review of a new drug application.

- Fast-track FDA review of designated qualified infectious diseases products.

- Intensified efforts to assist small businesses in conducting end-stage clinical trials through NIH small business awards.

- Tax Credits for R&D: Allows manufacturers of qualified infectious diseases products to take a tax credit equal to 35% of the qualified infectious diseases research expenses for the taxable year.

- Manufacturing Facilities Investment Tax Credit: Provides a tax credit of 20% for a facility that is used for manufacturing, distributing, or for research and development of a qualified infectious diseases product.

- Clinical Trial Guidelines for Antibiotic Drugs: Requires the FDA to issue guidelines, within one year, for the conduct of clinical trials with respect to antibiotic drugs, including antimicrobials to treat resistant pathogens, bacterial meningitis, acute bacterial sinusitis, acute bacterial otitis media, and acute exacerbation of chronic bronchitis.

To strengthen the bill further, IDSA would encourage the following incentives be considered:

- FDA Priority Review Voucher—Under this concept, a voucher would be provided to a company that obtains an approval for a "qualified product" that treats a disease identified by the Commission. The company could then apply the voucher to a separate product (i.e., a potential blockbuster) of its choosing or, alternatively, the company could auction the voucher to another company. The voucher concept was raised in the March/April 2006 edition of Health Affairs. The authors say that this concept may reduce FDA's review time of a product by a year, which could be worth "more than $300 million for a potential blockbuster". Even if the FDA review time was reduced only by 6 months, IDSA believes this concept would have merit. A significant advantage of this approach is that it would not extend the length of the patent. As such, it should not be a threat to the generics industry. Instead, it would permit a company to market a product months in advance of when it otherwise would. This also would be an advantage to patients as they would be able to enjoy the product's benefits sooner. The Health Affairs articles authors report the cost of changing FDA's review from standard to priority review may be $1 million, which could be recovered through a user fee by the voucher user. Of note, under the authors' approach, the company would have to forgo patent rights—this is an idea that IDSA does not support.

- Extension of Patent Term for Qualified Infectious Diseases Products—Although fraught with politics, the extension of the patent term of critical needed qualified infectious diseases products for 2 years or even 6 months is one sure way to pique industry's interest. There are so few solutions available to address the lackluster pharmaceutical pipeline for antibiotics and other antiinfectives. It may be time for Congress to consider this idea.

- Tax Credits for R&D—IDSA would suggest increasing the amount of the tax credit for R&D in the Cubin bill to 50% to mirror the amount provided to orphan drugs under the Orphan Drug Act. IDSA also would suggest applying this tax credit to preclinical research as well as product clinical research and development.

- Protocol Assistance—In addition to the development of clinical guidelines by FDA, we also would support the agency's provision of additional protocol assistance similar to what is provided with regard to orphan drugs.

- Waiver of User Fees—We would support the waiver of all user fees related to FDA review of qualified infectious diseases products.

- Antitrust exemptions—additional flexibility for certain company communications is needed.

- Guaranteed Market—While it can be loosely argued that Project Bioshield may be applied already to naturally occurring resistant organisms, it is not likely that the Administration will view such infections as priorities unless Congress strengthens its emphasis in this area.

- Funding for CDC's Antimicrobial Resistance Program—Although it may be outside the scope of the Subcommittee's reauthorization effort, we appeal to you to help strengthen CDC's resistance program so that the agency may better lead the nation to respond to the silent epidemic that antimicrobial resistance has created. A multi-pronged approach is essential to limit the impact of antibiotic resistance on patients and public health. For this reason IDSA supports *a $25 million increase in this program to a total commitment of $50 million in FY 2007.* This will enable CDC to expand its surveillance of clinical and prescribing data that are associated with drug-resistant infections, to gather morbidity and mortality data due to resistance, to educate physicians and parents about the need to protect the long-term effectiveness of antibiotics, and to strengthen infection control activities across the United States. Broadening the number of CDC's extramural grants in applied research at academic-based centers also would harness the brainpower of our nation's researchers.

Conclusion

The reauthorization of Project Bioshield provides a critical opportunity to spur the development of new tools to protect Americans and the global community against the

scourge of infectious diseases, particularly antibiotic resistant organisms, and bioterrorism. We urge congressional leaders to show bold leadership as it renews this legislation.

Specific to antibiotics, the past two decades of antibiotic development clearly have demonstrated that we no longer can rely on existing market forces to keep companies engaged in this area of drug discovery and development. Should additional companies' antibiotic R&D infrastructures be dismantled, it will take years to establish new programs—or this expertise could simply be lost forever. New antibiotics are desperately needed to treat serious as well as common infections. The bacteria that cause these infections are becoming increasingly resistant to the antibiotics that for years have been considered standard of care, and the list of resistant pathogens keeps growing. It is not possible to predict when an epidemic of drug-resistant bacteria will occur—but we do know it will happen.

Drugs, vaccines and diagnostics also are needed across the spectrum of infectious diseases medicine, including to address the growing threat of pandemic influenza. Conquering AIDS, TB, malaria, the neglected diseases found primarily in developing countries, and the next emerging infection will require renewed vision, creative policymaking and righteous action.

We appreciate the opportunity to testify. We look forward to working with you in the coming months to develop federal legislation to spur the tools infectious diseases physicians need to treat our seriously ill patients. Thank you.